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A FAST, "ZERO SYNAPSE" ACOUSTIC REFLEX: MIDDLE EAR MUSCLES PHYSICALLY SENSE EARDRUM VIBRATION

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A Study design/planning
B Data collection/entry
C Data analysis/statistics
D Data interpretation
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F Literature analysis/search
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Abstract

The middle ear muscles may be inconspicuous, but they are special. Silently standing guard at the entrance to the inner ear, their role is to spring into action whenever sound input rises, protecting the highly sensitive cochlea from overload. Such a task requires the utmost speed, for sounds can reach damaging levels within milliseconds. Neural-mediated mechanisms are slow, with the acoustic reflex arc taking up to a hundred milliseconds or more. Here, evidence is assembled that the middle ear muscles have recruited an additional, faster mechanism. The proposal is made that these muscles have developed a preflex mechanism – a zero-synapse system inherent to muscle fibres which, in response to vibration, rapidly stiffens the muscles. Preflexes are a developed form of sensitivity to perturbation common to all muscles, and have recently been identified in leg muscles, for example. However, the advantages that preflexes confer to an animal's auditory system have not yet been recognized. Applied to the middle ear muscles, heightened sensitivity to vibration means that any loud sound entering the middle ear causes the muscles to immediately stiffen, providing instant, on-the-spot overload protection. The muscles are therefore self-reflexive – they are both sensors and actuators. It is shown here how the middle ear muscles appear to have the special anatomical and physiological properties required for preflex action. There are strong resemblances to the superfast muscles of bats, birds, and fish, and to the fast flight muscles of insects.

Key words: muscle, stretch sensitivity, preflex, vibration

REFLEJO ACÚSTICO RÁPIDO DE "SINAPSIS CERO": LOS MÚSCULOS DEL OÍDO MEDIO FÍSICAMENTE CAPTAN LAS VIBRACIONES DEL TÍMPANO

Resumen

Los músculos del oído medio pueden pasar desapercibidos, sin embargo son excepcionales. Son los guardianes silenciosos del acceso al oído medio. Su papel es movilizarse cada vez que el sonido aumente, protegiendo la altamente sensible cóclea contra sobrecargas. Esta tarea requiere la máxima rapidez, dado que el sonido puede llegar a un nivel dañino en tan sólo milisegundos. Los mecanismos mediados por neuronas son lentos, produciéndose el reflejo acústico con una latencia de hasta cien milisegundos o más. Por lo tanto, en el presente trabajo se argumenta, en base a las evidencias recogidas, que los músculos del oído medio han adquirido un mecanismo adicional, más rápido. Se propone que dichos músculos han desarrollado el mecanismo de prerreflejo, un sistema de "sinapsis cero", propio de las fibras musculares que en respuesta a vibraciones tensan repentinamente los músculos. Los prerreflejos constituyen una forma de sensibilidad a trastornos típicos para todos los músculos y recientemente se han descubierto por ejemplo en los músculos de las piernas. Sin embargo, los beneficios proporcionados por los prerreflejos para el sistema auditivo en animales siguen sin reconocerse. En caso de los músculos del oído medio, su sensibilidad elevada a vibraciones significa que cualquier sonido que llega al oído medio hace que los músculos se atiesen inmediatamente, ofreciendo de esa manera una protección local y provisional contra sobrecargas. Los músculos son asimismo capaces de efectuar autorreflejos, actuando al mismo tiempo como sensores y activadores. El presente trabajo demuestra cómo los músculos del oído medio parecen contar con propiedades anatómicas y fisiológicas especiales, necesarias para que se produzca el prerreflejo. Se parecen claramente a los músculos superrápidos de los murciélagos, las aves y los peces, o bien a los músculos rápidos de los insectos.

Palabras clave: musculo, sensibilidad al estiramiento, prerreflejo, vibraciones

БЫСТРЫЙ АКУСТИЧЕСКИЙ РЕФЛЕКС «НУЛЕВОГО СИНАПСА»: МЫШЦЫ СРЕДНЕГО УХА ФИЗИЧЕСКИ ОЩУЩАЮТ ВИБРАЦИИ БАРАБАННОЙ ПЕРЕПОНКИ

Резюме

Мышцы среднего уха могут казаться скромными, но они исключительны. Они тихо стоят на стражи у входа во внутреннее ухо. Их роль – приступить к действию каждый раз, когда звук растёт, защищая необыкновенно чувствительную улитку внутреннего уха от перегрузки. Эта задача требует самой большой скорости, поскольку звук может достичь уровня, причиняющего вред, за миллисекунды. Механизмы с участием нейронов медленны, сам акустический рефлекс длится даже сто или

более миллисекунд. Поэтому также в настоящей работе были собраны доказательства того, что мышцы среднего получили дополнительный, более быстрый механизм. Предлагается, что данные мышцы развили механизм префлекса – систему нулевого синапса, свойственную мышечным волокнам, которые в ответ на колебания резко фиксируют мышцы. Префлексы являются развитой формой чувствительности к нарушениям, характерным для всех мышц, и были недавно открыты в частности в мышцах ног. Однако преимущества, какие префлексы обеспечивают слуховой системе у животных, ещё не были признаны. В случае мышц среднего уха повышенная чувствительность к колебаниям означает, что любой громкий звук, попадающий в среднее ухо, вызывает немедленный рост жёсткости мышц, обеспечивая экстренную, местную защиту от перегрузки. Таким образом, мышцы способны к авторефлексам, являясь как датчиками, так и активаторами. Здесь показано, как мышцы среднего уха, кажется, имеют специальные анатомические и физиологические свойства, необходимые для срабатывания префлекса. Они очень похожи на супербыстрые мышцы летучих мышей, птиц и рыб, а также быстрые мышцы насекомых.

Ключевые слова: мышца, чувствительность к растяжению, префлекс, колебания

SZYBKI ODRUCH AKUSTYCZNY „ZEROWEJ SYNAPSY": MIĘŚNIE UCHA ŚRODKOWEGO FIZYCZNIE WYCZUWAJĄ WIBRACJE BŁONY BĘBENKOWEJ

Streszczenie

Mięśnie ucha środkowego mogą wydawać się niepozorne, są jednak wyjątkowe. Stoją cicho na straży wejścia do ucha wewnętrznego. Ich rolą jest przystąpienie do działania każdorazowo, gdy dźwięk wzrasta, chroniąc niezwykle wrażliwy ślimak ucha wewnętrznego od przeciążenia. To zadanie wymaga najwyższej prędkości, jako że dźwięk może osiągnąć szkodliwy poziom w ciągu milisekund. Mechanizmy z udziałem neuronów są powolne, sam refleks akustyczny trwa nawet sto milisekund lub więcej. Dlatego też w niniejszej pracy zebrano dowody na to, że mięśnie ucha środkowego pozyskały dodatkowy, szybszy mechanizm. Proponuje się, że mięśnie te rozwinęły mechanizm prefleksu – system zerowej-synapsy właściwy włóknom mięśniowym, które w odpowiedzi na drgania raptownie usztywniają mięśnie. Prefleksy są rozwiniętą formą wrażliwości na zaburzenia charakterystyczne dla wszystkich mięśni i zostały ostatnio odkryte na przykład w mięśniach nóg. Jednakże zalety jakie prefleksy zapewniają systemowi słuchowemu u zwierząt nie zostały jeszcze uznane. W przypadku mięśni ucha środkowego, podwyższona wrażliwość na drgania oznacza, że dowolny głośny dźwięk docierający do ucha środkowego powoduje natychmiastowe usztywnienie mięśni, zapewniając doraźną, miejscową ochronę przed przeciążeniem. Mięśnie są zatem zdolne do auto-odruchów, są zarówno czujnikami, jak i aktywatorami. Pokazano tutaj, jak mięśnie ucha środkowego wydają się mieć specjalne właściwości anatomiczne i fizjologiczne niezbędne do działania prefleksu. Są wyraźnie podobne do superszybkich mięśni nietoperzy, ptaków i ryb oraz szybkich mięśni owadów.

Słowa kluczowe: mięsień, wrażliwość na rozciąganie, prefleks, drgania

Introduction

The middle ear muscles – the tensor tympani attached to the malleus and the stapedius attached to the stapes – are the smallest striated muscles in the human body. The bellies of the muscles are hidden away within the bone surrounding the middle ear cavity, so it is not surprising that the muscles have frequently been overlooked. Only their tendons project into the cavity and connect there with the ossicles – the three tiny bones, again the smallest in the body, which conduct sound from the eardrum to the cochlea.

It is clear that the muscles protect the cochlea from damaging sound levels, although how they do so is incompletely known. Various physical models have been proposed to explain their mode of action, but there is no universally agreed mechanism. The most widely accepted model is that the muscles stiffen the acoustic chain, increasing the acoustic impedance of the system (1, 2). An alternative theory is that the muscles increase fluid pressure in the cochlea, damping down the gain of the cochlear amplifier (3).

The purpose of this paper is not to weigh up these options but rather to consider how the protective mechanism is triggered: how the contraction of the muscles is initiated and how it can occur so rapidly that it is able to protect the cochlea from short, impulsive sounds. The paradox here is that the acoustic reflex is known to have a typical latency of about 100 ms (4), and sometimes shorter at high intensity (2), yet the loudest sounds in nature are impact sounds which have rise-times of milliseconds or less. The question is how the acoustic reflex could be useful in these circumstances. Indeed, Simmons (5) has framed the issue in evolutionary terms and has wondered what high-level sounds exist in nature which could possibly have driven the evolution of the middle ear muscle system. About the only high-level environmental sounds with long time-constants (many tens of milliseconds) are rolls of thunder, and deafeningly loud examples are so rare as to be a negligible evolutionary force.

Here we resolve the paradox by assembling evidence that the acoustic reflex occurs more quickly than currently recognized, and that internally generated sounds, such as from the larynx, can be surprisingly loud. The latency as measured by an electrode or tympanometer is only part of the story, and it is suggested that the effective latency is much shorter than measured by timing the muscle reflex arc. Like all vertebrate muscles, the middle ear muscles are sensitive to vibration, and so by becoming responsive to the vibration of the tympanic membrane, it is possible for them to act virtually instantaneously, avoiding neural delays. The system therefore incorporates a zero-synapse reflex loop, as well as the usual three- or four-synapse one (2). Indeed, the question might be asked what other muscle could more usefully employ inherent sensitivity to vibration than the tensor tympani and the stapedius?

There is evidence, both direct and indirect, that the middle ear muscles are capable of extremely short latencies. Based on psychophysical data in the literature, and inferences from the behavior of animals, it is concluded that the

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mammalian middle ear muscles contain an inherent 'preflex' mechanism known from certain other sets of muscles and which bypasses the usual multiple-synapse reflex loop (6, 7). Preflexes require a special muscle architecture, and draw on properties like those seen in the 'superfast' muscles of birds, bats, and fish, and resemble those of the 'indirect' myogenic muscles of insects. A bat uses superfast muscles in its larynx to emit 200 calls per second, while an insect can contract its wing muscles 600 times per second, giving credibility to the idea that the human middle ear muscles might have developed a comparable millisecond-scale performance. At root, the tensor tympani and the stapedius need to act with the utmost speed, and the evidence for how this might be achieved comprises the core of this paper.

The acoustic reflex: four anomalies

When a loud sound enters the auditory system, it triggers a reflex contraction of the middle ear muscles – the acoustic reflex – which in turn attenuates the conduction of sound to the cochlea (2, Ch. 8). A standard audiological measurement is the reflex threshold – the sound level required to elicit a change in the impedance of the ear measured with a tympanometer, and typically the threshold in normal subjects is taken to be 85 dB (2), although it has been recorded as low as 50 dB in humans (8), 35 dB in cats (9), and 20 dB in bats (10). The generally accepted explanation for how this protection is brought about is that the contraction stiffens the joints and ligaments in the ossicular chain, raising its mechanical impedance and lowering the sound input (2). An alternative explanation, the intralabyrinthine pressure (ILP) theory, describes how the force exerted by the muscles on the stapes raises the pressure of incompressible fluid within the otic capsule, and this pressure directly compresses outer hair cells and lowers the gain of the cochlear amplifier (3, 11). The ILP theory seeks to explain how the attenuation provided by the acoustic reflex can exceed 30 dB at frequencies below 1 kHz, whereas experiments and models often report very small figures, only a few decibels. This paper takes the ILP theory as the preferred model, and focuses on four anomalies surrounding the acoustic reflex which can be well accommodated by the ILP theory. The four anomalies are set out below.

First, there is the effect of impulse noise. When the latency of the acoustic reflex is measured, it is approximately 130 ms when recorded by an increase in impedance of an acoustic probe placed in the ear canal (4). It is shorter, but still at least 25 ms, when measured by an electrode inserted in the muscle (2). At the same time, there are people (and animals) who seem, paradoxically, to be relatively immune to the effects of high-level impulse noise lasting only a millisecond or so. For example, there are people with so-called 'hard ears' – boilermakers who have worked in very noisy industrial environments for decades without any apparent ill-effect on their hearing (12). Similarly, an experiment has been conducted where the middle ear muscles of cats have been disabled (by cutting the tendon which joins the muscles to the ossicles) and subjecting the animals to repeated gunfire at 145 dB (13). Remarkably, whereas the cats with disabled muscles averaged a permanent threshold shift of 44 dB, the cats with intact muscles suffered a loss of only about 5 dB, implying that the middle ear muscles were able to protect the ear from very loud, short impulses.

The second anomaly is the finding, not widely appreciated, that when pure tones are used as stimuli, the threshold for the acoustic reflex is *independent of hearing loss* (14, 15). That is, when a population of subjects is tested, some with hearing loss and some without, both groups have the same acoustic reflex threshold, at least up to a maximum loss of 70 dB (see Figure 1).

This is peculiar, for one might expect deafness to lead to a lower level of cochlear stimulation and hence a higher (poorer) acoustic reflex threshold, but this is not the case. On the other hand, if the trigger for the acoustic reflex resides not in the cochlea but in the middle ear muscles, then it is the absolute level of the sound input – the amplitude of physical vibration – which is the important parameter, and the sensation level becomes less important.

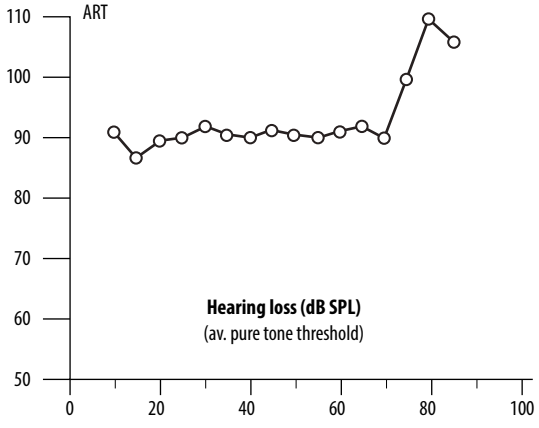

Figure 1. Evidence suggesting the acoustic reflex is not triggered by the cochlea. The horizontal portion of the plot illustrates the remarkable fact that the acoustic reflex threshold (ART, measured contralaterally and elicited by a pure tone in the ipsilateral ear) is *independent of hearing loss* up to 70 dB. A logical inference is that the reflex is triggered by the middle ear muscles themselves, whose vibration sensitivity is independent of the inner ear. The abscissa is average hearing threshold (at 0.5, 1, 2, and 4 kHz) among a pool of 1207 subjects. From (14) and used with permission

A third anomaly is seen in the behavior of echo-locating bats. These animals emit short, high-intensity ultrasonic calls, from which they detect faint echoes returning from prey, such as a moth or other flying insect. The calls must be loud in order to generate detectable echoes, but the problem is that the bat's cochlea must be protected from these intense sounds so as to preserve the utmost sensitivity. The solution used by the bat is to contract its middle ear muscles preceding and during a call, blanking out the pulse and reducing its loudness (16). This same mechanism is used by humans to facilitate conversation: the middle ear muscles contract when the person is speaking (and generating loud internal speech

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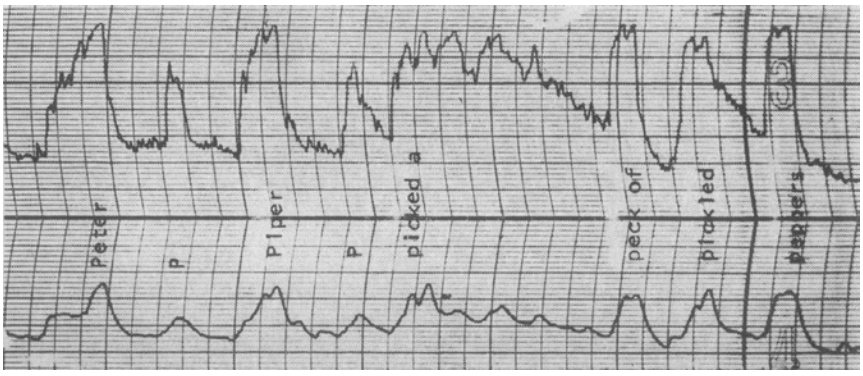

Figure 2. Parallel recordings of acoustic input impedance measured in the ear canal (top trace) and speech sound pressure level (lower) show that the two track each other almost instantaneously, demonstrating that the middle ear muscles contract and release very quickly (in less than a small fraction of a second). Time scale: 1 square is approximately 0.1 second. Reproduced from (19) with permission

sounds), but relax immediately afterwards in order to pick up the low-level reply. The result is a constant variation in muscle tension – a gain-control mechanism (17) – so as to effectively switch between being speaker and listener (18). This dynamic variation can be picked up with an impedance bridge, as shown in Figure 2 (19). In terms of the bat, the paradox is that the animal emits calls at up to 190 clicks per second (20) [see Figure 3], so the question becomes how can the animal turn its middle ear muscles on and off – that is, perform pulse-blanking – within a 5 ms time frame? The problem is exacerbated when one considers how it is possible for a bat to protect its ear from the calls of other bats nearby, and one neurophysiological investigation was unable to provide a satisfactory answer in terms of the latency requirements of a 5-synapse reflex arc (10).

Finally, consider the circumstances surrounding what is known as the reversed acoustic reflex. Unlike the normal acoustic reflex, which results in an increase in acoustic impedance, the reversed reflex shows a *decrease* in impedance. More interestingly, the reversed reflex is fast – it occurs within about 20 ms – and, even more curiously, it can be measured in deaf people, and even cadavers.

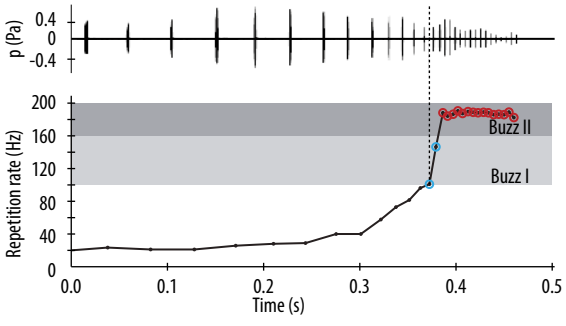

Figure 3. A train of sonar-like clicks (top) emitted by an echo-locating bat as it approaches its prey. The click rate starts out at 20 per second (bottom), but rapidly increases to 190 per second at encounter (the 'buzz' phase, grey shading). The time between clicks in the buzz phase is only 5–10 ms, requiring especially fast laryngeal muscles. Correspondingly, the bat also needs to contract and release its middle ear muscles at a similar rate in order to perform 'pulse blanking' – attenuating its loud call so as to prevent cochlear overload and allowing perception of returning echoes. From (20) and used with permission

Hypothesis: self-reflexivity of the middle ear muscles

The above anomalies can all be explained with one hypothesis: that the middle ear muscles are ultrafast muscles which rapidly stiffen due to an inherent sensitivity to vibration. As will be described, the muscles have special myogenic properties which permit this to happen – they have in-built 'preflexes' – and their architecture is not unlike the flight muscles of insects which permit mosquitoes to beat their wings up to 600 times per second. Unlike the displacement cycle of the mosquito's wing muscles, however, mammals do not have to move their middle ear muscles much: all that is required is an almost imperceptible isometric contraction, enough to exert tension on the ossicles and alter pressure in the otic capsule (or, according to the standard explanation, stiffen up ligaments). The following sections spell out the essential components of this hypothesis.

Vibration sensitivity of muscle

It is known that all muscles are, to some degree, sensitive to vibration. When high-frequency vibration, even of small amplitude, is applied to a muscle, it is a potent stimulus for eliciting contraction (21). Known as the tonic vibration reflex, the contraction is attributed to excitation of proprioceptive muscle spindles (22). Muscle spindles are part of a servo-mechanism involved in regulating muscle length (23). Muscles have various muscle receptors able to respond to stretch (spindle primary endings), length (spindle secondary endings), and tension (Golgi tendon organs) (24). One explanation for the vibration sensitivity of muscle is that it may originate from a ratchet mechanism involving cross-bridges between actin and myosin in muscle fibres (25).

Regardless of the mechanism, a point that has tended to be overlooked is that the vibration sensitivity of muscle is, for one reason or another, extremely high. For example, one early study (21) found that soleus muscle spindles could be driven to fire by low-frequency vibrations (less than 200 Hz) of just 3 μm peak to peak (Fig. 3 of (21)). More recent work (24) in human volunteers found vibration thresholds of leg muscles of about 100 μm at frequencies below 100 Hz. The significance of these small displacements is amplified when the relative stretch of the muscle fibres is considered. A 3 μm stretch in a 3 cm soleus muscle corresponds to an extension of the muscle by

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about 1 part in 10,000, and in terms of the length of the individual muscle fibres by about 1 in 40,000. As Brown and colleagues emphasise (p. 798), a 1 μm stretch corresponds to a displacement of just 40 nm of the innervated region. The same calculation for the long leg muscles produces a similarly small number.

At this point, a comparison should be made with the amplitude of vibration of the eardrum in response to sound. At 80 dB SPL, the human eardrum undergoes a peak-to-peak displacement of about 100 nm at 1 kHz (26). At the same time, the eardrum is attached, via the malleus, to the tensor tympani. Given the vibration sensitivity of human leg muscle just mentioned, it appears possible that a muscle with short fibres – the fibres of the tensor tympani are only 1 mm long – could readily sense vibration of the eardrum resulting from an 80 dB sound. A 100 nm stretch of a 1 mm fibre is 1 part in 10,000, which could easily be sensed by a muscle, suggesting that a much lower threshold for the tensor tympani may well be possible. A threshold of 60 dB SPL corresponds to a stretch of 1 part in 100,000, and this might be possible for such a specialised muscle to detect, as later discussion sets out. This is the hypothesis explored here: that the tensor tympani can be activated, not just neurogenically by efferent nerve impulses as conventionally understood, but immediately and rapidly by the mechanical vibration of the eardrum, to which it is attached. Such an idea was suggested by Filogamo (23), but does not appear to have gained traction. The possibility that proprioceptive elements were involved in activatating the middle ear muscle reflex was also mentioned by Eliasson and Gisselsson (27).

The clear advantage of this mechanism is ultimate speed: instead of a reflex loop involving multiple synapses and long delays, there are zero synapses and virtually no delay. Moreover, it is on-the-spot, so contraction of the muscle occurs where it is needed, increasing input impedance and, more significantly, increasing intralabyrinthine pressure. Without appreciable delay, the outer hair cells are hydraulically squeezed by the fluid in the cochlea surrounding them and their gain is thereby attenuated (3).

Of course, there are drawbacks to this arrangement, and one of them is a possible hypersensitivity to sound input, eliciting contraction when it is not needed. From this perspective it is worth noting there is a condition called 'self-induced vertigo' in which a person suffers nystagmus and dizziness from just talking, humming, or from loud external sounds – sometimes even from playing a violin (28). Clinically, this is known as the Tullio phenomenon (28), and can even be observed in congenitally and profoundly deaf subjects (29). In a related condition, vibration applied directly to the mastoid can also produce nystagmus (30). Sometimes just an increase in ear canal pressure will, via inwardly directed motion of the ossicles, increase pressure in the otic capsule and cause vertigo (Hennebert's sign (31)). Tellingly, just a touch to the face can occasionally induce vertigo (28), strongly suggesting involvement of the middle ear muscles (probably the tensor tympani). Hennebert's sign is rare in patients with otosclerosis, pointing to the need for a mobile stapes footplate in order to allow hydraulic pressure to increase. A recent paper (11) assembles additional evidence in support of the ILP theory, explaining how inward motion of the stapes could affect balance as well as hearing, and suggesting that Meniere's disease might therefore arise as a dysfunction of the middle ear muscles. A number of other factors come into play too, but the main point is that balance can be disrupted by activity of the middle ear muscles, the tensor tympani being the most probable locus. A possible unifying scenario, therefore, is that the middle ear muscles might be directly sensitive to vibration and are effectively self-reflexive. Not only would such sensitivity be useful in speeding up the acoustic reflex, bypassing a number of synaptic circuits, but it also has major implications for understanding a number of hearing and balance disorders.

With this idea in mind, there are several additional factors which can be identified as contributing to this enhanced sensitivity and speed, and these will now be addressed.

Preflexes: the effect of nonlinear viscoelasticity

The idea that muscles are able to inherently spring into action without any neural intermediary is already established in the literature, although the term 'preflexes' for the phenomenon, introduced by Loeb (6), is not so common. Loeb used preflexes to refer to self-stabilisation of muscle against external perturbation, a behaviour that can be attributed to intrinsic nonlinear viscoelasticity – a purely physical property which effectively creates a zero-delay feedback loop. In the context of muscle dynamics, the term "thixotropic" has also been applied to the property by which muscles, through displacement of their spindles, offer different resistance to small and large movements (25).

Nishikawa and colleagues (32) describe how when an external load changes unexpectedly, the total stiffness (or, more generally, impedance) of the system will adjust automatically and instantaneously without requiring neural input due to the load-dependent nonlinear stiffness

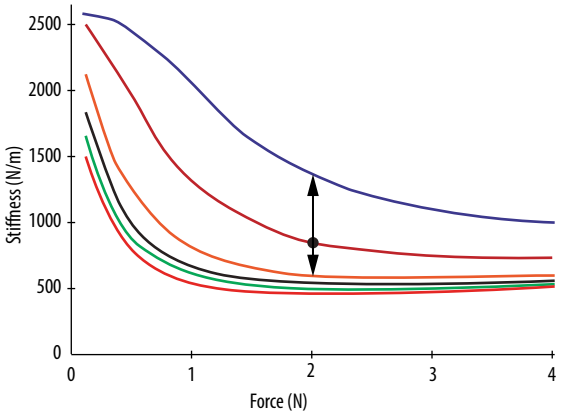

Figure 4. How the stiffness of a muscle changes nonlinearly with load. If the external load increases, the stiffness increases (upward arrow), but if the load decreases the stiffness decreases (downward arrow). The nonlinearity in response tends to stabilise the muscle's position. From (32) and Lappin et al. (2006); used with permission

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of actively shortening muscle (Figure 4). The muscle becomes stiffer when the external load increases, and less stiff when it decreases, a result which is likely to affect the acoustic impedance of the ear as measured in the ear canal by a tympanometer.

Preflexes have been observed in many muscle systems, especially those involving antagonistic muscle pairs, where they act together to stabilise the system against perturbation (7). Examples that have been studied include contractions of the leg and shoulder. An animal might step into a hole while running, for example, and a preflex allows the leg to accommodate instantaneously, preventing a trip. At the microscale, the exact mechanism behind preflex action remains unclear because experimental techniques to observe sarcomeres and cross-bridges during contraction have necessarily been indirect (33). Nevertheless, Nishikawa and colleagues attribute much of the nonlinearity to the mechanical properties of intrafusal fibres (32)

Normally, the passive and active stiffnesses of these fibres are modified by neural control, but their non-neural responses, while potentially significant, are often hidden away. However, it is known that muscle spindles themselves are nonlinear, and are more sensitive to stretch than to release. They are particularly sensitive to small rapid changes in length, and so are especially responsive to vibration (32, p.22). Vibration is thought to act directly on the muscle's contractile machinery to reduce its viscous resistance to stretching, perhaps by rupturing cross-bridges and therefore adding a component of negative viscosity (34). In vivo, cross-bridges are continually being broken and remade.

The usefulness of preflexes to the middle ear muscle system has not yet been appreciated, despite their clear advantages in terms of speed and stability. A preflex would prevent the eardrum, and the entire ossicular chain, from undergoing sudden displacement in response to a loud sound. That is, a preflex would prevent the stapes from impulsively moving within the oval window, protecting the cochlea from sudden spikes in pressure. The effect is physical, so there is no need for neural reflex loops and their associated delay.

Unique anatomy of the middle ear muscles

The anatomy of the middle ear muscles is unique. They are the smallest striated muscles in the human body (6 mm for the stapedius and 20 mm for the tensor tympani (35)). Being striated means that, as well as being activated by reflexes, they should be under voluntary control. Indeed, many people are able to voluntarily contract their middle ear muscles, and even the anticipation of a loud sound can elicit a contraction (36). The nerve pathways and relay stations are unclear, and even the question of whether the stapedius and tensor tympani act as synergists or antagonists is still undecided (37, 38). Functional studies by Klockhoff (39) indicate that the stapedius and tensor tympani work antagonistically, although it seems the stapedius is activated purely by sound, whereas the tensor tympani is activated by speech, chewing, swallowing, yawning, and touch to the face or ears.

In humans, sound does not appear to activate the tensor tympani, at least not by standard neural means. Some have even proposed that the tensor tympani is a vestigial muscle and performs no useful function (40). The acoustic reflex probably involves three or four synapses, although shorter, more direct, connections have been demonstrated whose physiological relevance is not known (38). There is still much about these muscles that remains to be discovered.

In the light of what was said earlier about the stretch threshold of muscle spindles, the most important anatomical property of the middle ear muscles is that the fibres are extremely fine and short, only 1–2 mm (41). Based on a length of 1 mm and a 10 nm peak-to-peak vibration of the eardrum at 60 dB SPL, that means such a sound level would stretch the muscle spindles by 1 part in 100,000. This fraction should be compared with the 1 part in 40,000 for ordinary soleus muscle which, as pointed out earlier, demonstrably causes contraction. The middle ear muscles operate virtually isometrically, working against the compliance of the round window; displacements of up to 50 μm are usual (11), but a figure of 1 nm has been cited as being of functional significance (p.31 of (35)).

The geometry of the fibres within the middle ear muscles needs to be recognised. The middle ear muscles belong to the class of pennate muscles whose fibres are arranged like a feather (Fig. 5). An interesting implication of pennate muscle architecture has been investigated by Azizi and colleagues (42). Significantly, the middle ear muscles are surrounded by bone, and so when the muscle fibres contract, the muscles are not able to expand, so the fibres are forced to rotate. As the figure illustrates, contraction of the fibres then provides increased force but reduced displacement. A parallel is the powerful claws of the lobster, which are also driven by pennate muscles.

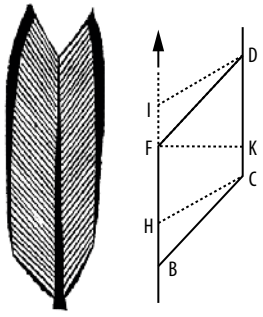

Figure 5. A pennate muscle, such as a middle ear muscle, and its fibre geometry. The muscle is surrounded by bone, and so its cross-section (FK) must stay constant. When a muscle fibre contracts (e.g. DF to DI), it acts like a lever, providing high force but little displacement. From (42) with permission

Histologically, the tensor tympani shows a very unusual combination of short fibres whose function is not immediately apparent, but the fibres comprise a mix of fast-twitch fibres (type IIM), rare slow tonic fibres, and some slow-twitch fibres (41). Slow tonic fibres are common in birds, but in mammals they are confined to the extraocular muscles, larynx, masseter, and middle ear muscles (43). A feature of slow tonic muscle fibres is that they are short and do not contract with a twitch like other muscle fibres. Instead, they undergo slow and prolonged shortening, making them resistant to fatigue and well suited to prolonged isometric contraction. Another distinctive

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property noted by Han and colleagues is that slow tonic fibres may work together with muscle spindles to enhance proprioception (43). In this way, the entire muscle might be considered an extended sensory unit, and that therefore the function of the muscles could plausibly be sensory – sensitive not only to position but also to vibration.

The middle ear muscles are rich in myosin and ATPase, and are well suited to contraction for long periods without fatigue. This is consistent with the idea that the muscles can sustain a continuous isometric force, as required by the intralabyrinthine pressure hypothesis. This function is supported by the other places where muscles rich in slow tonic fibres are found: the thyroarytenoid muscle in the larynx (which must finely regulate vocal cord tension for speech and song) and the extraocular muscles (to accurately position the eyeball for visual fixation). Studies of the proprioceptive spindles in the middle ear muscles show a dense concentration of motor and proprioceptive nerve fibres, with each motoneurone innervating about six muscle fibres (38, 44). Curiously, however, electromyographic studies in which an electrode is inserted into the tensor tympani show virtually no electrical activity in response to sound. One interpretation is that the muscle plays only a minor role in the acoustic reflex (38), but another possibility is that the muscle is a special type – a 'superfast' muscle – which in intrinsically vibration-sensitive and self-reflexive.

Superfast muscle

The fibre composition of the middle ear muscles is similar to that of another class of highly specialized muscle known as superfast muscle. This muscle type is defined by its ability to quickly contract – more than 100 times a second – and is found in the laryngeal muscles of echolocating bats, the corresponding syrinx of birds, the shaker muscle of the rattlesnake, and the sonic muscles of toadfish (20). The proposition put forward here is that the middle ear muscles are also superfast muscles capable of very rapid contraction.

The classic example of a superfast muscle is the laryngeal muscles of echo-locating bats. As mentioned earlier, these animals generate sonar-like pulses at up to 190 per second from their throat, and these ultrasonic, high-intensity clicks (up to 130 dB) allow the bat to catch flying insects based on the returning echoes (20). The massively enlarged laryngeal muscles are under neural control, and the high tension produced across a vocal membrane in the throat generates ultrasonic vibrations. If the bat emits a call every 5 ms, then a very fast on and off cycle is required – on the scale of a millisecond – and this is what superfast muscle is designed to do. The rapid cross-bridge kinetics of the fast fibres have been the subject of study (45, 46), but the details are not entered into here.

Of greater interest are the implications of an active superfast laryngeal muscle for the bat's middle ear muscles. In general, it is known that when the laryngeal muscles of any animal are activated for speech production, the middle ear muscles simultaneously contract, attenuating loud internally generated sound and keeping the cochlea sensitive to incoming external sounds. So if the bat's laryngeal muscles contract at 190 times a second, the middle ear muscles are also expected to contract at that speed (16). The logic of this was pointed out by Hartridge more than 60 years ago (47). Hartridge – who was the first to suggest that bats used ultrasound for echolocation – drew an analogy to pulse-blanking used in radar and sonar, where the extremely large outgoing pulse is apt to severely overload the receiver circuitry needed to detect the echo, in which case a long time is needed before sensitivity can be regained. The answer is pulse-blanking: attenuating the receiver circuit at the same time as the pulse is being produced, preserving sensitivity for the returning echo. In the same way, Hartridge suggested that the bat uses its middle ear muscles to attenuate cochlear sensitivity simultaneous with the production of its ultrasonic call (47). The solution means that bats activate their middle ear muscles and laryngeal muscles at matching rates, switching them on and off within milliseconds (16). This arrangement makes sense of the observation that the middle ear muscles in bats are enormously large relative to the size of the animal (p.135 of (48)). In this context, it is of interest that the belly of the tensor tympani in humans – some 20 mm – is in fact larger than the cochlea itself, but whether this muscle too is in the superfast category needs further research. The bat's enhanced performance also explains why it has a direct acoustic pathway from the larynx to the cochlea (the stylohyal bone (49)), since bone has a high sound conduction speed which helps provide the shortest possible latency.

Superfast muscle is not just found in bats. The syrinx of birds (analogous to the mammalian larynx) allows songbirds such as the starling to create virtuoso vocalization, and this anatomical specialty is also controlled by superfast muscle (50, 51). Other examples of animals with superfast muscle are catfish and toadfish. These animals activate muscles to rapidly drum on their swimbladders, producing bursts of sound, and the muscle responsible – the ventral sonic muscle – is of the superfast type (52). Interestingly, the vocal apparatus of several species of catfish also includes other muscles – the dorsal sonic muscle (in doradids) and the tensor tripodis (in pimelodids) – whose contraction protects the fish's inner ear from overload during vocalization. The tensor tripodis is a small conical muscle attached to the first of the Weberian ossicles (53), the three tiny bones connecting the swim bladder to the inner ear. Named in analogy to the tensor tympani, and acting similarly, the tensor tripodis prevents the fish's inner ear from being overloaded when the fish is drumming its swimbladder to communicate. The tensor tripodis contains thin myofibrils, many mitochondria, and short sarcomeres (53). Whether it is a superfast muscle is again a matter for further investigation, but circumstantially it probably is.

The fast flight muscles of insects

Every skeletal (striated) muscle in vertebrates is synchronous, meaning that each twitch is preceded by an action potential and that calcium ions must be released and later re-sequestered by the sarcoplasmic reticulum in order to complete a contraction cycle (52). Superfast muscles are no exception, and to increase speed, small fibres are

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used to accelerate calcium build-up. Force and speed are inversely related, so it follows that the short fibres and isometric force output of middle ear muscles are helpful in allowing them to control intralabyrinthine pressure at high rates.

Of course, synchronous activation has its limits, and the question arises as to whether asynchronous activation, as used in insect flight muscles, might allow even higher contraction rates in the auditory system (54, 55). Using asynchronous muscle, insects are able to beat their wings at prodigious rates, up to 600 Hz in the case of mosquitoes. A detailed treatment of how insect muscle achieves such high rates is not entered into here (but see overviews in (56, 57)). However, it is worth noting that insects contract their flight muscles at multiples of the nerve impulse rate by stimulating the muscles indirectly. The insect makes use of an associated mechanical resonance – such as from vibration of its thorax – to act as a pacemaker for muscle contraction. That is, like a quartz crystal in an oscillator circuit, it uses the vibration of the thorax, and the sensitivity of the wing muscle to stretch supplied by that vibration, to keep its wings beating (57-60). Marden highlights a difference between the "big dumb power-producing muscles" in insects and their "small smart steering muscles" which are capable of rapid and finely graded responses (57). It helps that the mosquito and its muscles are small, so the stretch the muscles undergo is relatively large.

This paper makes the case that the mammalian middle ear muscle may be a small steering-like muscle, and could use stretch derived from vibration of the tympanic membrane to induce contraction. In this case, however, the contraction is tonic, not phasic, but nevertheless the response is still rapid. It may be that the middle ear muscles use some of the mechanisms employed by asynchronous muscle to increase speed, and one of them may be abandoning the need for sequences of nerve impulses to cause contraction. The lack of electrical activity seen in electrode recordings of the tensor tympani – as in recordings of the DSM muscle of toadfish (52) – gives support to this possibility.

There is one striking example which demonstrates how the middle ear muscles have combined extreme vibration sensitivity with utmost speed, and this is the case of the inverted acoustic reflex.

The case of the inverted acoustic reflex

For decades there has been a curious anomaly in acoustic reflex measurements: if a loud sound is applied to an ear, in certain circumstances an unexpected *decrease* of acoustic impedance, rather than the expected increase, is sometimes recorded. The anomalous response is fast – as low as 20 ms – and can be recorded in people who are deaf, and even in cadavers (61). No wonder, therefore, that the 'inverted acoustic reflex' or 'reversed ipsilateral acoustic reflex' (RIAR) has been dismissed by some as an equipment artefact (61-63), even though others think it is a real physiological event (64, 65). The explanation offered here is that the response is real: it is the result of loud sound directly causing the tensor tympani to contract, and this is seen as a reduction in impedance in the ear canal recorded by the tympanometer. In this regard, even excised muscle is subject to vibration-induced shortening (66), explaining how responses can be recorded in cadavers. Significantly, in one study which tended towards the artefact view (63), the median 'artefact' threshold measured in cadavers turned out to be about the same as the real acoustic reflex threshold measured in normally hearing subjects, or in a subject having total hearing loss. This suggests either that there are considerable measurement errors or that the artefact is systematic and has not been fully accounted for.

The RIAR has regular on and off times (about 20 ms and 150 ms respectively), just like the normal acoustic reflex does (61), but is only seen ipsilaterally when the stapedius is nonfunctional (as in cases of otosclerosis or stapedectomy). It can be observed under anesthesia, after neuromuscular block, as well as in deaf and dead subjects. It appears with the same shape and time constants in people with otosclerosis, profound deafness, facial paralysis, acoustic neuroma, or dislocated ossicles (64, 67). It is not seen in every subject, which it would do if it were an equipment artefact, does not appear in a hard test cavity, and does not start and end with the stimulus as other artefacts do (65). Faced with this conundrum, some have suggested the tympanic membrane may be responsible (68, 69), but such a proposal has not solved the problem. The paradoxical responses persist with different equipment and different frequencies. However, responses do require free movement of the eardrum and malleus, implicating the tensor tympani (65, 70).

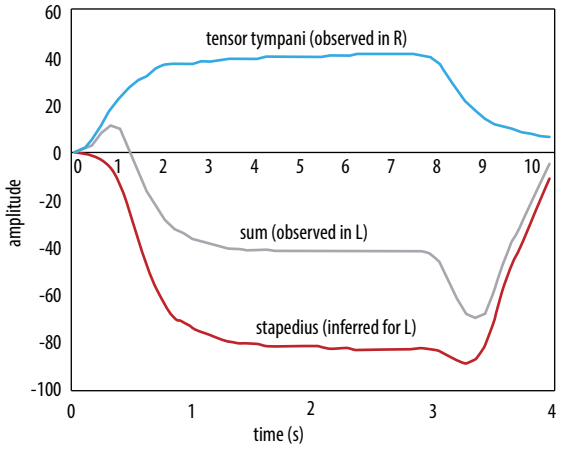

Figure 6. Separating the effects of the tensor tympani and the stapedius from unilateral acoustic reflex measurements in a patient with one otosclerotic right ear and one normal left ear. The right ear gives a response indicative of the tensor tympani (blue); the left ear gives the presumed sum of both middle ear muscles (grey). The algebraic difference reveals the inferred action of the stapedius (red). The plot explains why reflex action of the tensor tympani is frequently overwhelmed by the action of the stapedius, the only sign of its presence being a small upward deflection, frequently overlooked. Adapted from Fig. 3 of (65)

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The hypothesis tying all these observations together is that loud sound applied to the ear stimulates the tensor tympani muscle directly (via its vibration sensitivity) and causes a sudden decrease in impedance. In this way, vibration produces similar effects to electrical stimulation of muscle. Indeed, it is well known that alternating electrical currents applied to dead muscles (as in a meat carcass) cause shortening, and so it is not unexpected that vibration operates similarly – explaining the cadaver findings.

Evidence that the RIAR is a real response, and not an artefact, comes from studies which found the RIAR in all 44 patients who lacked a normal ipsilateral acoustic reflex (65). This study compared the profile of the RIAR over time in these patients with the profile of the ipsilateral acoustic reflex in subjects with normal hearing, looking particularly at onset and offset times. Their findings were that the RIAR was just the positive component of the normal ipsilateral reflex, which has both positive and negative components. They showed that the normal ipsilateral reflex could be fitted with two exponential components of opposite sign and with different onset and offset latencies. As shown in Figure 6, there is an initial upward deflection (decrease in impedance) which is soon countered by a later downward deflection (increase in impedance). This biphasic behavior can be interpreted to mean that otosclerotic patients lacked the negative component (because their stapes had undergone fixation), leaving only the upward component.

Ciardo and colleagues suggest that the upward deflection can be associated with contraction of the tensor tympani and that the negative deflection is due to the stapedius, a proposal suggested decades earlier (71, 72). The present paper supports such an interpretation. Contraction of the tensor tympani causes a decrease in impedance (increase in admittance), while contraction of the stapedius does the opposite. Under normal circumstances, the upwards deflection is largely hidden by the downwards, but by taking the difference between the two traces, and making assumptions about continuity, it is possible to isolate the two components, and these are also shown in Fig. 6. It can be seen that the total increase in impedance as normally measured (the sum of the two traces) may in fact be considerably smaller than that displayed by each of the muscles individually. That is, the tensor tympani reflex is normally masked by the action of the stapedius, but as Fig. 6 indicates, it is possible to unmask the tensor tympani reflex by separating the two response profiles algebraically.

Why did the tensor tympani's role remain hidden for so long? One reason appears to be that the tensor tympani reflex is ipsilateral (and positive-going), while the stapedius reflex is bilateral (and negative-going). Most studies on the acoustic reflex have been made on normal subjects using a contralateral stimulus – experimentally it's easier to do (otherwise there's overlap and a pulse-blanking problem to be taken care of). That means the larger stapedius reflex always overwhelms the tensor tympani reflex – unless ipsilateral studies on otosclerotic subjects are conducted. In fact, some researchers have already implicated the tensor tympani in explaining the biphasic features of the acoustic reflex (72). Another factor preventing recognition of its pivotal role has been that the tensor tympani is primarily elicited by non-acoustic stimuli: it involves the facial nerve and is usually stimulated by chewing, speaking, yawning, touch to the face, startle, and conscious effort. Finally, of course, there has been no consideration that the tensor tympani might be activated non-neurally – by physical vibration.

In summary, the unifying hypothesis of this section is that vibration directly triggers middle ear muscle contraction. Such a fast reaction would also, of course, benefit the stapedius as much as the tensor tympani, and the suggestion here is that this is probably the case.

Concluding comments

Assembling a wide range of evidence, this paper has argued that the unique anatomy and physiological properties of the middle ear muscles are aimed at making them intrinsically sensitive to vibration – that is, they are self-reflexive. When sound levels approach damaging levels, the muscles instantly stiffen, protecting the cochlea from overload. A neural transmission loop is unnecessary (although of course available as a slower, supplementary mechanism); with zero synapses, protection can be in place within milliseconds.

Because the muscles are cryptic and act almost isometrically, these guardians of the cochlea work silently and invisibly, and their activity can easily be overlooked. Whereas impedance changes can be seen using tympanometry when the stapedius contracts, changes due to contraction of the tensor tympani are comparatively small and are not always evident. Although the action of the tensor tympani may be elusive, it is still an important component of the acoustic reflex. It is not true that the tensor tympani is vestigial and unimportant in protecting the cochlea (40). Evidence is largely indirect and has here been extrapolated from general findings about the vibration sensitivity of muscle in other animals. The most direct evidence comes from studies of the inverted acoustic reflex, which to date has usually been dismissed as an artefact. It is suggested that further studies of this anomaly could enlarge our understanding.

The rate of ultrasonic calls made by bats is remarkable, and the hypothesis put forward is that their superfast laryngeal muscles are complemented by equally fast middle ear muscles. In this scenario, the middle ear muscles perform 'pulse blanking' which prevents the receiver (the cochlea) from being overloaded by the transmitter (the click from the larynx). This neat solution, as found in standard sonar and radar practice, no doubt improves the bat's echolocation performance and is worth investigating in detail. Translated to the human situation, the inference is that our middle ear muscles also perform fast gain-riding, attenuating loud internally generated speech in order to allow fainter, external conversation to be perceived. People who have undergone tenotomy (cutting of the tendon of the middle ear muscles) complain of the excessive loudness and 'tinniness' of their own voice (5). Patients with Meniere's disease also frequently complain of a difficulty in following speech (73).

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The reconsiderations explored in this paper enlarge the role of the middle ear muscles considerably, and present them as part of a fast, high-finesse control loop. The middle ear muscles make use of many of the principles already identified under the term preflexes, but display them in a faster and more sophisticated form. The limits to the performance of the middle ear muscles raise fundamental physical and physiological issues.

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